UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	**PAPER NUMBER**
	4

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/386,591	NEEDLEMAN ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,12,13 and 22-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,12,13 and 22-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a))

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

Claims 3-7, 12, 13, and 22-39 are pending in this application.

Priority

1. This application is a continuation of 08/934367, filed 09/19/97, and a continuation-in-part of 08/785997 and 08/788882, both filed 01/21/97. The instant claims, drawn to DNA vaccines, represent new material added in application 08/934367 and the application therefore has a priority date of 09/19/97.

Information Disclosure Statement

2. The information disclosure statement received on March 7, 2000 lists references contained in applications 08/785,997, 08/788,882, and 08/934,367. Application 08/934,367 is not available and the references included therein have not been considered, with the exception of U.S. patents and available foreign documents.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 3, 6, 7, 26, 29, 30, and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et al. in view of Francis and Clarke.

Thomas et al. (J. Allergy Clin. Immunol., vol. 99, no. 1, p. S187, January 24, 1997) teaches the use of a plasmid-based vaccine encoding regions of CETP to generate anti-CETP antibodies in rabbits and thus raise HDL cholesterol levels, and suggests the use of similar vaccines in humans. Additionally, Thomas et al. teaches the use of the CMV promoter/enhancer and linking of two regions of CETP to a tetanus toxoid fragment. Thomas et al. further teaches intramuscular injection resulting in decreased serum cholesterol and protection against aortic lesions in rabbits placed on a high-cholesterol diet. Thomas et al., however, fails to teach the use of hepatitis B core antigen instead of tetanus toxoid to increase immunogenicity. Francis and Clarke (Methods in Enzymology, vol. 178, pp. 659-676, 1989) teaches the use of hepatitis B core antigen fused to a peptide epitope to induce production of antibodies. It would have been *prima facie* obvious to one of ordinary skill in the art to combine the methods of Thomas et al. with those of Francis and Clarke to replace the tetanus toxoid fragment taught by Thomas et al. with DNA encoding the hepatitis B core antigen of Francis and Clarke to produce the vaccine of claims 3, 29, 30, and 35. One of ordinary skill in the art would have been motivated to do so because Thomas et al. teaches a CETP DNA vaccine and Francis and Clarke teaches an art-standard method for optimizing

immunogenicity of vaccines. Claim 36 depends from claim 35; the use of a range of doses for therapeutic agents is art standard. Claims 6, 7, and 26 depend from claim 3 and specify mammalian species. Claim 6 specifies human, as specifically mentioned in Thomas et al. It would therefore have been obvious to apply the teachings of Thomas et al. to humans for the reason described in Thomas et al., to prevent or treat atherosclerosis in humans. Claim 7 specifies rabbit, as specifically taught by Thomas et al. Claim 26 specifies monkey. While monkey is not specifically taught by Thomas et al., the use of monkeys as animal models is art standard and it would therefore have been prima facie obvious to one of ordinary skill in the art to apply the teachings of Thomas et al. and Francis and Clarke to monkey, in order to produce an animal model for the use of a CETP DNA vaccine to treat atheroscelrosis in humans. Claim 34 depends from claim 3 and specifies injection into muscle or skin; intramuscular injection is specifically taught by Thomas et al.; intradermal injection is art standard.

5. Claims 3, 6, 7, 22, 23, 26-31, and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rittershaus and Thomas in view of Donnelly et al. and further in view of Francis and Clarke.

Rittershaus and Thomas (WO 96/34888, November 2, 1996) teaches peptide-based vaccines derived from CETP to treat atherosclerosis. Rittershaus and Thomas also specifically teach the use of the C-terminal 26 amino acids of CETP and fragments thereof, encompassing SEQ ID NOs: 10, 24, and 39 of the instant application as set forth in the instant claims 22, 23, 27, 28, and 33. However, Rittershaus and Thomas

fails to teach DNA vaccines or the use of hepatitis B core antigen to enhance immunogenicity . Francis and Clarke teach the use of hepatitis B core antigen as set forth above, but does not teach the injection of DNA to produce the antigenic peptides. Donnelly et al.(J. Immunological Methods vol 176, pp. 145-152, 1994) teaches DNA vaccines and provides methods for optimizing same. It would have been obvious to one of ordinary skill in the art to combine the teachings of Rittershaus and Thomas with those of Francis and Clarke and Donnelly et al. to produce a DNA vaccine for CETP using hepatitis B core antigen to enhance immunogenicity. One of ordinary skill would have been motivated to do so because of the improved immunogenicity resulting from the use of hepatitis B core antigen described by Francis and Clarke and the simplicity and effectiveness of DNA vaccines, as discussed by Donnelly et al.

6. Claims 4, 5, and 37-39 are rejected under U.S.C. 103(a) as being unpatentable over Thomas et al in view of Francis and Clarke as set forth above and further in view of Donnelly et al. (J. Immunological Methods vol 176, pp. 145-152, 1994).

Claims 4 and 5 depend from claim 3 and add the limitation of repeated injections. The use of repeated injections of a DNA vaccine is taught by Donnelly et al. to induce production of antibodies. It would have been obvious to one of ordinary skill in the art to use repeated injections of the vaccine described in claim 3 as described by Donnelly et al. One of ordinary skill in the art would have been motivated to do so in order to further optimize the vaccine of Thomas et al. to produce antibodies to decrease CETP levels. Claims 37-39 specify the use of saline, sucrose, or liposomes as a vehicle for

CETP DNA vaccines. Thomas et al. and Francis and Clarke teach as set forth above but do not teach specific vehicles. The use of these vehicles and their reported effects on DNA vaccine efficiency are taught by Donnelly et al. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings of Donnelly with those of Thomas et al. and Francis and Clarke to use different vehicles for CETP DNA vaccines. One of ordinary skill would have been motivated to do so because of the reported advantages of each set forth in Donnelly et al.

7. Claims 12, 13, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et al. in view of Brown et al.

Claim 12 and dependent claims 13 and 32 specify that the HBcAg be fused to both amino and carboxy termini of the antigen. Thomas et al. teaches a CETP DNA vaccine as set forth above but fails to teach hepatitis B core antigen linked at both ends to increase the immune response. Brown et al. (Vaccine, vol. 9, 595-601, 1991) teaches increased immunogenicity resulting from linkage of a rhinovirus peptide with HBcAg at both ends, as compared to linkage at the amino terminus only. It would have been obvious to one of ordinary skill in the art to combine the teachings of Thomas et al. with those of Brown et al. to link CETP or sequences thereof to HBcAg at both ends to increase the immune response to CETP. One of ordinary skill would have been motivated to do so in order to optimize the production of CETP antibodies and lower the level of CETP in an animal.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3-7, 12, 13, and 22-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The use of the phrase "cholesteryl ester transfer protein" and the abbreviation "CETP" in claims 3-7, 12, 13, and 22-39 are vague and indefinite because they only describes a protein of interest by an arbitrary name. While the name itself may have some notion of the activity of the protein, there is nothing in the claim that distinctly identifies the protein. Others in the field may isolate the same protein and give it an entirely different name or give the same name to a different protein. Applicant should particularly point out definitive characteristics associated with the protein with reference to an entered sequence. Describing biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly identify what the protein is.

Claim 12 is further rejected as referring to "said antigenic carrier". No antigenic carrier was previously mentioned. Claim 13 refers to "said encoded fusion protein", which was not previously mentioned. Claim 28 depends from claim 35, which is improper.

Claim 3 is further rejected as being internally inconsistent. In the preamble, the process is described as for increasing the concentration of HDL in the blood, while in (b) the stated goal is a decrease in HDL.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 3-7, 12, 13, and 22-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-7, 8-11, and 15-31 of copending Application No. 08/934367. Although the conflicting claims are not identical, they are not patentably distinct from each other because the sole distinctions between them are the incorporation of size limits on the length of either the CETP immunogen or the antigenic carrier, and the nature of the antigenic carrier.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (703) 308-3995. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via internet email regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published

in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet L. Andres, Ph.D.
May 15, 2000

YVONNE EYLER, PH.D
PRIMARY EXAMINER